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EXPERIMENTAL STUDIES ON FAT METABOLISM BEFORE AND AFTER OPERATION

by

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Received for publication Jan. 8, 1962

I. INTRODUCTION

Rapid advances in the field of surgery depend not only upon improvement in operative technique, anesthesia and excellent antibiotics, but also upon reform of nutritional management. By means of adequate administration of various nutriments (protein, carbohydrate, vitamins and salts), indications for operation have been extended markedly and the majority of postoperative complications has been prevented. Accordingly, recovery of surgical patients and healing of operative wound have been accelerated. However, clinical detailed investigations on pre- and post-operative administration of fat, which is a high caloric nutriment, have been hardly performed. Rather surgical patients have not been habitually supplied fat as a caloric source.

Recently it has been clarified that fat, especially essential fatty acids, have an important nutritional effect, and administration of it has been given attention.

HIKASA and his co-workers have succeeded in the production of a fat emulsion which can be infused intravenously.[1,12,13,14,15,16] Using this fat emulsion they have investigated the metabolic process of fat in vivo and applied it to surgical cases with satisfactory results.[9,23]

In surgical cases we must consider the following facts:

The majority of surgical patients is in a state of malnutrition, which must be corrected prior to operation, and they are destined to receive insults such as anesthesia or operation. Furthermore they are obliged to restrict their oral intake of diet for some period before and after operation. So it is a most important problem to investigate whether the administration of fat is effective or not in these surgical patients. ROBERTS, SAMUELS[31,32,33,37] and HANAFUSA[3] asserted that high fat diet must be adequately given to the patients who would be operated or they will be starved. MATSUDA,[25] who examined the liver glycogen level in starved rats, agrees with them.

Nowadays it has been clarified that glycerides, both absorbed from the intestine and mobilized from dépot fat are converted to phospholipids, which are transferred into the tissue cells in the form of α- and β-lipoprotein. These phospholipids play an important role as a constant and variable element of tissue cells. FUJINO[8] studied the influence of anesthesia on the first step of fat metabolism from the view-point of phospholipid formation. In this paper the influence of operation on phospholipid formation and fat adaptation effect, which was obtained by preoperative administration of fat emulsion, were reported by the use of radioactive P^{32}. Namely, it was investigated, whether pre- and post-operative administration of fat to surgical patients is effective or not.

Ⅱ. MATERIALS AND METHODS

1) Experimental animals: Healthy adult dogs weighing approximately 10kg were used in this study. They were placed on a standard diet for one week prior to operation, the composition of which is listed in Table 1. On the day of operation and the lst day after operation, they were fasted. On the 2nd day after operation 1/5 dose of the standard diet was given and it gradually increased to the whole quantity on the 6th day after operation. As the surgical procedure, gastrectomy (Billroth Ⅰ) was performed under intravenous anesthesia with a 2.5% solution of Ravonal. At the onset of the experiment the dogs were in the so-called post-absorptive state in which the fat contained in the diet was not absorbed from the intestine and mobilization of dépot fat had not yet occurred.

Table 1 Diet on the dogs which received gastrectomy

	−7 −6 −5 −4 −3 −2 −1	0 ↓ gastrectomy 1	2	3	4	5	6 7 10 14
Diet	S. D.	fasting	S.D. × 1/5	S.D. × 2/5	S.D. × 3/5	S.D. × 4/5	S. D.

S. D.: standard diet rice 17gr (60 Cal) per Kg. b. w.
fish meal 4gr (10 Cal) 〃
water 40cc 〃
water 40cc

2) Radioactive phosphorus: Radioactive phosphorus in the form of $Na_2H\overset{*}{P}O_4$ was injected in the gluteal muscles of experimental animals in a dose of 0.5 mc per kg of body weight.

3) Fat emulsion: A 20% sesame oil emulsion, produced in our laboratory, was used. This emulsion contains various higher fatty acids in the form of mixed glycerides.

Table 2 Drugs for intravenous administration

Fat emulsion infused group	20% Fat emulsion (containing 7% glucose)	2cc	per kg b. w.
	5% glucose solution	8cc	〃
	Ringer's solution	10cc	〃
	Vitamins*		
control group	7% glucose solution	2cc	〃
	5% glucose solution	8cc	〃
	Ringer's solution	10cc	〃

* Vitamins Vitamin B_1 10mg Vitamin B_2 10mg
Vitamin B_6 30mg Vitamin C 100mg

In the fat infused group, this fat emulsion was administered repeatedly in a dose of 2 cc per kg of body weight with carbohydrates, salts and vitamins simultaneously (as shown in Table 2) for one week prior to operation. In the experiment for the measurement of phospholipid formation from glycerides, we used a single infusion of 5cc per kg of body weight of this emulsion 3 hours after the injection of P^{32}.

4) Collection of serum : After the administration of the fat emulsion, 10cc of blood was removed from the dogs on successive times such as 20 minutes, one hour and 2 hours after. The plasma was separated by centrifugation.

5) Preparation of animal tissue : As it has been clarified by our precursor that the amount of phospholipids in tissue reaches its maximum 3 hours after the administration of fat emulsion, so in the present experiments the animals were sacrificed by bleeding 3 hours after the infusion. The liver, kidney and heart muscles were removed for study, since these organs oxidize fat more actively than the other organs.

6) Preparation of acid-soluble and lipid phosphorus in serum and tissue : This was performed by the method of SCHMIDT and THANHAUSER.[38][42]

7) Determination of phosphorus : The method of FISKE and SUBBAROW was performed,[5][25][34][35] using an electrophotometer (BECKMAN's type) at a wave-length of 620mμ.

8) Measurement of the radioactivity : A part of each fractions obtained from (6) was transferred to a metal dish 3 cm in diameter. After drying, the radioactivity was measured by a GEIGER-MÜLLER's counter (Kobe kogyo K. K.) at 1250 volt.

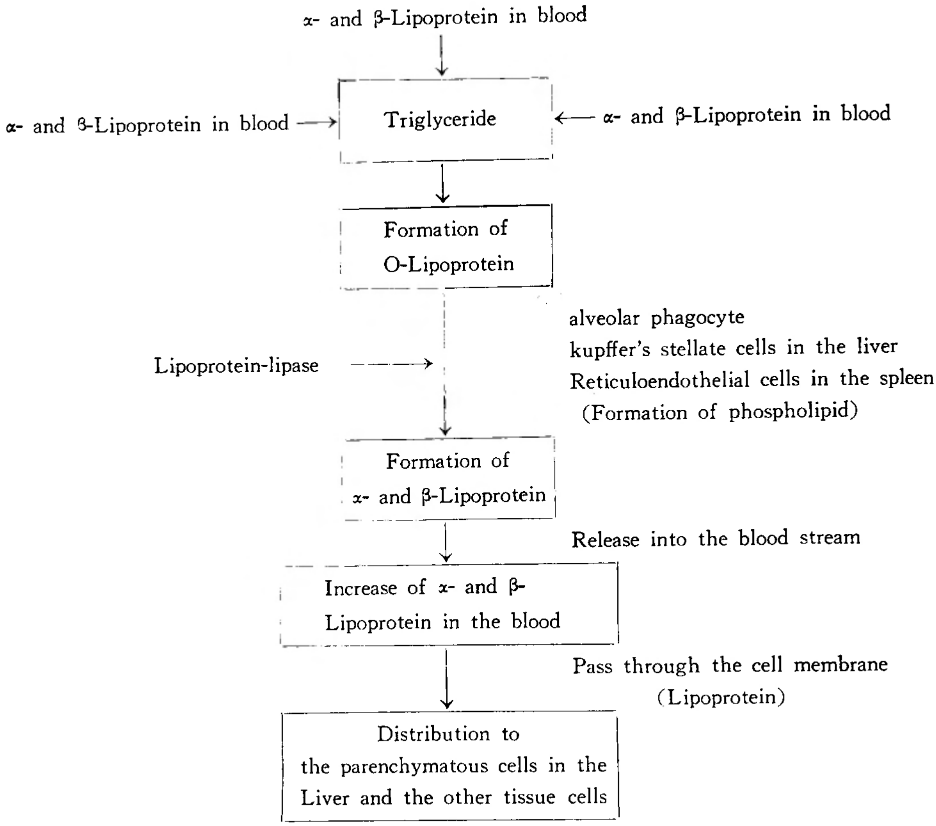
III. RESULTS

1) The phospholipids formed from the infused glycerides after infusion of the fat emulsion and the introduction of phospholipids labeled with P^{32} into tissues (preparatory experiment).

As mentioned above, it has been clarified that phospholipids play a very important role in fat metabolism. From these fact many investigators have used phospholipids as an indicator for study of fat metabolism.[2][4][5][7][11][31][33][43][44] In our laboratory, using the fat emulsion which could be infused intravenously, IKEDA,[19] NAKATA,[28] SENO[33] and KUYAMA[23] confirmed in vivo that the intravenously infused fat globules in the form of glycerides were phagocytized by alveolar phagocytes, KUPFER's cells of the liver, reticulo-endothelial cells of the spleen, and were converted to phospholipids in order to be metabolized effectively. Furthermore, ONISHI[30] and EUJINO[5], applying radioactive phosphorus and paper electrophoresis, studied the fate of infused glycerides and obtained the following result :

When the fat emulsion was administered intravenously, α-lipoprotein in serum, which had a high density and contained lipids in small quantities, gathered together around the infused fat corpuscles (triglyceride), and formed O-lipoprotein, which had low density and contained lipids in large quantities, and then glycerides were stabilized in the blood. Then, the stabilized glycerides were phagocytized by the above mentioned cells in which glycerides changed into phospholipids and they entered again into the blood stream in the form of α-and β-lipoprotein, not in the free form, and were carried to all the tissues through the blood stream. Thus it has been clarified that the infused glycerides were

Fig. 1 Fate of glycerides flowed into blood vessels



introduced to all tissues in the form of lipoprotein. The amount of phospholipids introduced into the tissues was largest in the liver. To make sure of the phospholipid formation from the infused glycerides in vivo, FUJINO's experiment was reexamined as a preparatory experiment using radioactive phosphorus. After a single intravenous infusion of a 20% sesame oil emulsion in a dosage of 5 cc per kg of body weight into animals in the post absorptive state, serum was collected on successive times and specific activities (abbreviated S A) of acid-soluble and lipid P^{32} were measured (Table 3). As shown in

Table 3 Turn over rate of lipid P in the serum following the infusion of fat emulsion

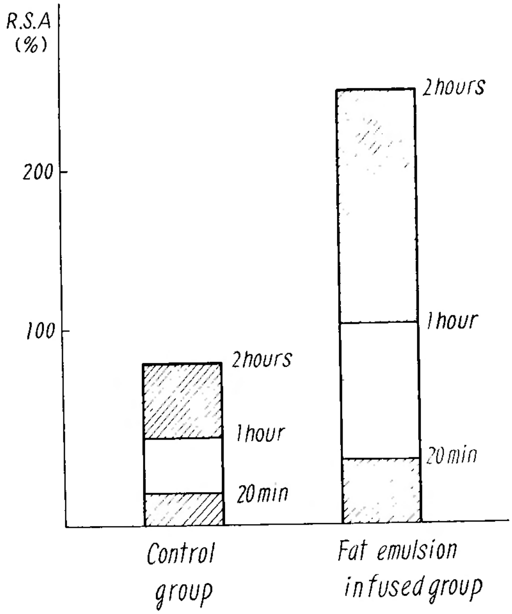
Intervals after infusion	Fat emulsion infused group			Control group		
	S. A.* of acid-sol. P	S. A. of lipid P	R. S. A.+ (%)	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. (%)
Before	71 (± 0)	9.0 (± 0)	12.7 (± 0)	69 (± 0)	9.3 (± 0)	13.5 (± 0)
20 min. after	59 (−17)	9.9 (+10)	16.8 (+32)	60 (−13)	9.4 (+ 1)	15.7 (+16)
1 hour after	45 (−37)	11.5 (+28)	25.5(+101)	51 (−26)	9.9 (+ 6)	19.4 (+44)
2 hours after	36 (−49)	15.5 (+72)	43.0(+239)	41 (−41)	10.1 (+ 9)	24.6 (+82)

(mean values)

* Specific activity : counts × 10^{-3}/min/mg

\+ Relative specific activity S. A. of lipid P/S. A. of acid-soluble P this Table, the S A of acid-soluble P^{32} showed a decrease of about $40\sim50\%$ in the course of the experiments, and no significant difference was observed between the fat emulsion infused group and the control group. On the other hand, the S A of lipid P^{32} increased in both groups, but much more in the fat emulsion infused group. Namely, the S A of lipid P^{32} showed only a 9% increase in the control group, but a 72% increase in the emulsion infused group. Using the relative specific activity (abbreviated R S A) to compensate for the variability from animal to animal,[42][44] it showed an increase of 82% in the control group and a 239% increase in the fat infused group, and a significant difference was observed in the both groups (Fig. 2).

Fig. 2 Changes in the relative specific activity of lipid P in the serum following the infusion of fat emulsion



Therefore, it may be considered that the remarkable increase of the S A of lipid P^{32} in the emulsion infused group is due to the active formation of phospholipids from the infused glycerides, that the metabolic process of fat in vivo is performed smoothly, and that the phospholipids, which were produced actively by the above mentioned organs, enter into blood stream abundantly. Eventually, we may be able to take these phenomena as an indicator which shows an ability to metabolize fat. According to our colleagues,[20][23][40] the amount of phospholipids in tissues reaches its maximum about 3 hours after the infusion of the fat emulsion. In the following experiments, therefore, the S A of acid-soluble P^{32} and lipid P^{32} in tissues was measured 3 hours after infusion. The liver, kidney and heart muscle were the organs selected for this study because of the previously mentioned reason (Table 4). The S A of lipid P^{32} increased two fold more in the emulsion infused group than in the control. This fact indicates the degree of the introduction of phospholipids into the tissues from the blood stream. In this experiment, the amount of phospholipids introduced into the tissues in the form of lipoprotein was largest in the liver. These results quite agree with those obtained by FUJINO, and represent

Table 4 Turn over rate of lipid P in tissues 3 hours after the infusion of fat emulsion

Organs	Fat emulsion infused group			Control group		
	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. (%)	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. (%)
Liver	86	51	59.3	89	29	32.6
Kidney	82	32	39.0	91	25	27.4
Heart muscle	90	9.5	10.5	87	4.0	4.6

(mean values)

Table 5 Influences of gastrectomy on turn over rate of lipid phosphorus in the serum following the infusion

(Fat not infused group before operation)

	Intervals after infusion	Before	Days after gastrectomy 1	2	3	5	7	10	14
S. A. of acid-soluble P × 10^{-3}	Before	78 (± 0)	62 (± 0)	61 (± 0)	63 (± 0)	68 (± 0)	74 (± 0)	79 (± 0)	75 (± 0)
	20 min. after	65 (−16)	51 (−17)	52 (−15)	57 (−10)	63 (− 7)	65 (−12)	66 (−16)	62 (−17)
	1 hour after	47 (−39)	43 (−31)	45 (−26)	48 (−24)	52 (−24)	53 (−28)	47 (−38)	44 (−41)
	2 hours after	38 (−51)	38 (−40)	38 (−38)	39 (−38)	41 (−40)	39 (−47)	39 (−50)	37 (−51)
S. A. of lipid P × 10^{-3}	Before	10.8 (± 0)	9.6 (± 0)	8.9 (± 0)	8.2 (± 0)	10.3 (± 0)	11.0 (± 0)	10.7 (± 0)	10.5 (± 0)
	20 min. after	12.0 (+11)	10.0 (+ 4)	9.4 (+ 6)	9.7 (+18)	12.4 (+20)	12.8 (+16)	11.9 (+11)	11.5 (+10)
	1 hour after	13.1 (+21)	10.4 (+ 8)	9.8 (+10)	10.2 (+24)	14.6 (+42)	14.9 (+35)	13.0 (+21)	12.6 (+26)
	2 hours after	19.7 (+82)	11.5 (+20)	10.5 (+18)	12.0 (+46)	15.3 (+49)	16.8 (+53)	16.5 (+54)	17.7 (+68)
R. S. A. (%)	Before	13.9 (± 0)	15.5 (± 0)	14.6 (± 0)	13.0 (± 0)	15.1 (± 0)	14.8 (± 0)	13.5 (± 0)	14.0 (± 0)
	20 min. after	18.3 (+32)	19.5 (+25)	18.1 (+24)	17.0 (+31)	19.7 (+30)	19.7 (+33)	17.7 (+31)	18.5 (+32)
	1 hour after	27.8 (+100)	24.2 (+56)	21.8 (+49)	23.3 (+79)	28.1 (+86)	28.2 (+90)	26.5 (+96)	28.6 (+104)
	2 hours after	51.8 (+273)	29.7 (+92)	27.6 (+89)	30.7 (+136)	37.3 (+147)	43.1 (+191)	42.1 (+212)	47.8 (+241)

(mean values)

evidently an aspect of the phospholipid formation from the infused glycerides in vivo.

2) The influence of gastrectomy on fat metabolism and the effects of the repeated intravenous administration of fat emulsion for one week prior to operation.

It has been noted that dépot fat is mobilized as the result of an operative insult such as a gastrectomy, enters into blood stream in the form of glycerides, and then is introduced into the metabolic process of fat. In order to clarify the changes in the metabolic process of fat following an operation, the author observed the influence of an operative insult on fat metabolism from the view-point of the phospholipid formation by using an intravenous administration of the fat emulsion. At first, the control dogs, fed with the standard diet as shown in Table 1, were infused repeatedly with carbohydrates and salts (Table 2) for one week before operation and then were gastrectomized. The S A of acid-soluble P^{32} and lipid P^{32} in serum were measured (Table 5) on the successive days after operation. The S A of acid-soluble P^{32} always showed a decrease of about 40~50% and a significant difference was not observed between specimens taken before and after operation. On the contrary, the S A of lipid P^{32} only reached an increase of about 20% on the lst and 2nd days after operation, although we observed about an

80% increase before operation. Also, the increase in the S A of lipid P^{32} in the serum following an infusion of fat emulsion had the tendency to return gradually to the preoperative level. Moreover, these facts became more evident by calculating the R S A (Fig. 3). Namely, the R S A of lipid P^{32} in serum following the infusion of the fat emulsion showed a 273% increase before operation, but only about a 90% increase on the lst and 2nd days after operation. Thus it has been observed distinctly that the phospholipid formation showed a marked decrease after operation and 2 weeks after operation it could not recover to the preoperative level.

From the above results, it was clarified that an operative insult markedly reduced the phospholipid formation from the infused glycerides in vivo. By measuring the S A and R S A of phospholipids labeled with P^{32} in the tissues, it was also clarified that the

Fig. 3 Changes in the relative specific activity of lipid phosphorus in the serum 2 hours after infusion (Influences of gastrectomy)

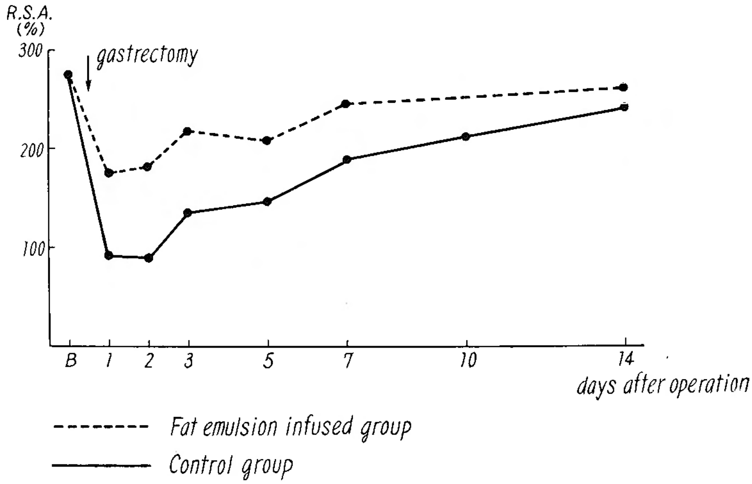


Table 6 Influences of gastrectomy on turn over rate of lipid phosphorus to the tissues 3 hours after the infusion
(Fat not infused group before operation)

	Organs	Days after gastrectomy							
		Before	1	2	3	5	7	10	14
S. A. of acid-soluble $P \times 10^{-3}$	Liver	91	82	78	88	93	102	92	90
	Kidney	80	67	72	75	85	81	96	91
	Heart muscle	83	80	75	80	86	92	85	75
S. A. of lipid P $\times 10^{-3}$	Liver	56	33	32	45	50	53	54	57
	Kidney	38	21	21	28	32	31	39	40
	Heart muscle	9.1	6.3	5.8	8.3	7.5	8.0	6.8	7.2
R. S. A. (%)	Liver	61	40	41	51	54	52	59	66
	Kidney	48	31	29	37	38	38	40	44
	Heart muscle	11	8	8	10	9	9	8	9

(mean values)

introduction of phospholipids into the liver, kidney and heart muscle were remarkably reduced after operation, especially in the liver (Table 6 & Fig. 4). Namely, the introduction of phospholipids labeled with P^{32} into the above mentioned organs on the lst and 2nd days after operation showed a reduction to 2/3 of the preoperative level.

One should consider in observing these results that since an operative insult such as a gastrectomy disturbs markedly the formation of phospholipid from the infused glycerides in vivo, it also reduces remarkably the introduction of the produced phospholipids into the various organs. On the other hand, when the fat emulsion (2 cc/kg b. w.) was

Fig. 4 Changes in the relative specific activity of lipid phosphorus to the tissues 3 hours after infusion (Influences of gastrectomy)

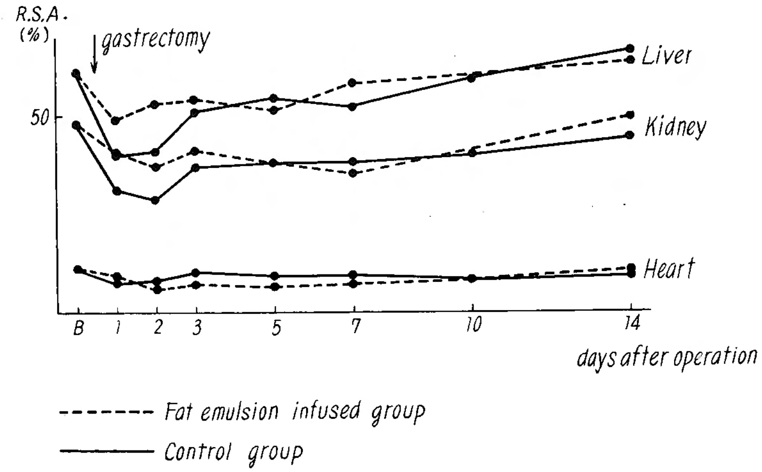


Table 7 Influences of gastrectomy on turn over rate of lipid phosphorus in the serum following the infusion
(Fat and vitamins infused group before operation)

	Intervals after infusion	Days after operation 1	2	3	5	7	14
S. A. of acid-soluble $P\times10^{-3}$	Before	65 (± 0)	70 (± 0)	76 (± 0)	78 (± 0)	72 (± 0)	75 (± 0)
	20 min. after	56 (−14)	64 (− 9)	65 (−14)	69 (−12)	65 (−10)	68 (− 9)
	1 hour after	45 (−31)	55 (−22)	53 (−30)	58 (−26)	54 (−25)	55 (−27)
	2 hours after	38 (−42)	41 (−41)	39 (−49)	43 (−45)	37 (−49)	38 (−49)
S. A. of lipid P $\times10^{-3}$	Before	8.3 (± 0)	9.3 (± 0)	10.3 (± 0)	10.2 (± 0)	10.0 (± 0)	9.8 (± 0)
	20 min. after	9.1 (+ 8)	10.5 (+13)	11.9 (+16)	12.0 (+18)	11.9 (+19)	11.5 (+17)
	1 hour after	10.7 (+29)	12.0 (+29)	14.0 (+36)	14.6 (+43)	15.2 (+52)	14.2 (+45)
	2 hours after	13.1 (+58)	14.3 (+54)	16.9 (+64)	17.5 (+72)	17.8 (+78)	18.0 (+83)
R. S. A. (%)	Before	12.8 (± 0)	12.4 (± 0)	13.6 (± 0)	13.1 (± 0)	13.9 (± 0)	13.1 (± 0)
	20 min. after	16.3 (+27)	16.4 (+32)	18.3 (+35)	17.4 (+33)	18.3 (+32)	16.9 (+29)
	1 hour after	23.9 (+56)	21.8 (+76)	26.4 (+94)	25.2 (+92)	28.1(+102)	25.8 (+97)
	2 hours after	35.5(+177)	34.9(+181)	43.3(+218)	40.7(+209)	48.1(+245)	47.4(+262)

(mean values)

given with carbohydrates, salts and vitamins, simultaneously (as shown in Fig. 2), the decrease of the phospholipid formation from the infused glycerides on the lst and 2nd days after operation were far slighter than in the control group. Its recovery was so rapid that the preoperative level was observed one week after operation in the fat infused group (Table 7 & Fig. 3).

These results indicate that: Though an operative insult always disturbs the formation of phospholipid from the infused glycerides, abundant administration of fat and various vitamins prior to operation is effective for making a favourable environment for utilization of the dèpot fat smoothly. Therefore, the dogs which were infused repeatedly with the fat emulsion and the various vitamins are able to recover from surgical operation sooner than the control group.

3) Comparison of the fat emulsion infused group and the vitamin infused group.

In order to clarify whether the cause of the favourable influence on the post-operative fat metabolism depends upon the preoperative administration of vitamins or fat, the following examination were carried out under identical conditions.

The animals were divided into 2 groups. The first group was infused the fat emulsion (2cc per kg b. w.) containing carbohydrates and salts repeatedly for one week. The second group was infused with vitamins combined with carbohydrates and salts. The dogs of both groups were then gastrectomized. The phospholipid formation from the infused glycerides on the 2nd day after operation, when it was disturbed to a maximum degree, was compared in both groups. Furthermore, the introduction of P^{32}-labeled phospholipids into the various organs was investigated (Table 9, 10). R S A was illustrated graphically in Fig. 5. As shown in Fig. 5, the R S A of lipid P^{32} in the serum following the infusion of the fat emulsion on the 2nd day after operation showed a 164% increase in the I group, which was the same order of magnitude compared with the fat and vitamins infused group and only a 17% difference was observed between them. It should be considered therefore that the phospholipid formation from the glycerides is not disturbed considerably by the preoperative administration of fat and is maintained at a

Table 8 Influences of gastrectomy on turn over rate of lipid phosphorus to the tissues 3 hours after the infusion
(Fat and vitamins infused group before operation)

	Organs	Days after operation					
		1	2	3	5	7	14
S. A. of acid-soluble $P \times 10^{-3}$	Liver	90	86	79	94	78	80
	Kidney	79	82	85	86	82	79
	Heart muscle	82	102	93	91	80	85
S. A. of lipid P $\times 10^{-3}$	Liver	44	46	43	48	45	51
	Kidney	32	30	35	33	29	39
	Heart muscle	7.2	6.2	6.5	6.4	5.9	8.3
R. S. A. (%)	Liver	49	53	54	51	58	63
	Kidney	41	37	41	38	35	49
	Heart muscle	9	6	7	7	7	10

Table 9 Turn over rate of lipid phosphorus in the serum in 2 experimental groups (which show values on the 2nd day after gastrectomy)

Intervals after infusion	I group *			Ⅱ group +		
	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. %	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. %
Before	73 (± 0)	8.9 (± 0)	12.2 (± 0)	64 (± 0)	9.5 (± 0)	14.8 (± 0)
20 min. after	64 (−12)	9.8 (+10)	15.3 (+26)	54 (−16)	9.9 (+ 4)	18.3 (+24)
1 hour after	51 (−30)	10.7 (+20)	21.0 (+72)	47 (−27)	10.3 (+ 8)	21.9 (+47)
2 hours after	43 (−41)	13.8 (+35)	32.2(+164)	39 (−39)	11.4 (+20)	29.2 (+97)

(mean values)

* I Group : Glucose + Ringer's sol. + Fat emulsion

\+ Ⅱ Group : Glucose + Ringer's sol. + Vitamins

Table 10 Turn over rate of lipid phosphorus in tissues in 2 experimental groups (which show values on the 2nd day after gastrectomy)

Organs	I group			Ⅱ group		
	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. %	S. A. of acid-sol. P	S. A. of lipid P	R. S. A. %
Liver	85	39	46	101	40	40
Kidney	92	31	33	82	29	35
Heart muscle	104	9.8	9.0	93	8.1	8.7

(mean values)

level as high as the normal. On the other hand, in the Ⅱ group, it showed only a 97% increase. It is obvious that the preoperative administration of the vitamins is not effective for improvement of postoperative disturbances in fat metabolism.

A remarkable difference between the I group and the Ⅱ group was also observed by investigating the introduction of lipid P^{32} into tissues. The above results indicate that preoperative administration of fat emulsion plays a most important role in preventing the disturbance of phospholipid formation which occurs inevitably after operation.

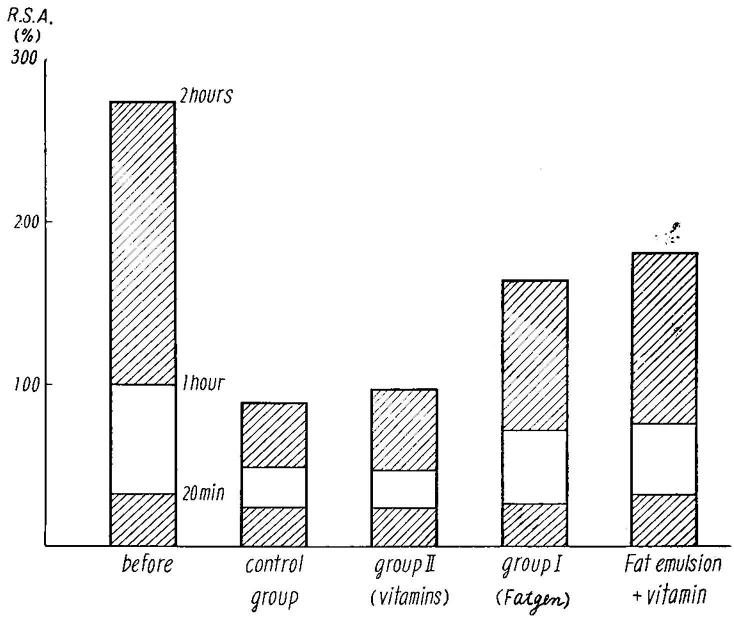
Ⅳ. DISCUSSION

The influence of an operative insult on the metabolic process of fat in vivo, especially on the formation of phospholipids from the infused glycerides was investigated in these experiments. Evidence has been obtained to support the theory that disturbance of the phospholipid formation after operation was markedly improved by the abundant administration of fat preoperatively.

According to SELYE's general adaptation theory, it is gradually believed that destruction of body protein, increased urinary nitrogen excretion, retention of sodium and chloride and loss of potassium following an operative insult are a series of phenomena of stress response.

Concerning fat metabolism, it has been noted that dépot fat is mobilized and decreases rapidly as a result of an operative insult. Consequently, the total fatty acid content in the blood increases, the phospholipid level in the blood and liver decreases markedly, and

Fig. 5 Changes in the relative specific activity of lipid phosphorus in the serum in various experimental groups
(on the second day after gastrectomy)



thus the dépot fat is mobilized and introduced into the metabolic processes in the body.

There is, however, some disagreement as to whether all of these changes in fat metabolism could be regarded as stress response. Some investigators reckon them as only a secondary phenomenon due to a loss of carbohydrate and protein. Thus even concerning the explanation of these phenomena, there is as yet no definite agreement, so that we can accurately decide whether the disturbances of the phospholipid formation from the infused glycerides following an operation, as observed in these experiments, can be regarded as stress responses or secondary phenomena due to a lowering of the functions of the body, especially liver function.

From the results that the metabolic process of fat were improved remarkably and performed smoothly with the preoperative administration of the fat emulsion, it may be considered that not all of the postoperative disturbances in fat metabolism can be regarded as stress response. Accordingly, if the various nutriments, especially the reasonable fats, were administered sufficiently prior to operation and the liver function was improved and protected, the glycerides mobilized from dépot fat are smoothly introduced into the process of the fat metabolism in vivo as follow: In the form of α- and β-lipoprotein, as described before, they are introduced into all tissues of the body and some of them contribute to the construction of tissues and fulfilment of living functions as constant elements, and the others are oxidized smoothly to be used as a caloric source. By what mechanism do these phenomena occur? A most significant fact is that what plays a very important role in the improvement of postoperative disturbance of fat metabolism is not the administration of vitamins but fat itself. Consequently, we should consider that these phenomena are due to the special nutritional effect of fat.

ROBERTS and SAMUELS demonstrated that animals maintained on diets high in carbohydrate or fat exhibited a preferential utilization of the foodstuff which constituted the predominant source of calories in the diet. This adaptation to fat feeding was evidenced during subsequent fasting as a higher rate of acetone body excretion, a slower rate of disappearance of blood sugar level and a lowered rate of nitrogen excretion.[32)33)]

Using C^{14}-labeled acetate, WHITENEY et al. revealed the fact that in animals fed with high fat diets the depletion of liver glycogen is minimized in the fasting period and the blood sugar levels are maintained at higher levels than the group fed with another predominant foodstuff.[41)]

These facts show directly that the dietary history of animals is an important factor for determining the apportionment between their stored carbohydrate and fat which can be utilized during fasting. Therefore, since the main storage-nutriment is fat, the abundant supply of fat before fasting is a most favourable procedure.

These facts were also clarified by MATSUDA's experiments, which investigated the glycogenolysis of the liver in starved rats, the liver glycogenesis of rats following the administration of glucose solution and the gluconeogenesis in starvation.

These experiments suggest that the metabolic pattern of animals, which have been fed with a diet predominant in carbohydrate, is characterized by an exceedingly high rate of carbohydrate utilization in fasting and the liver glycogen is depleted rapidly. On the contrary, in animals fed with a high fat diet, such a metabolic tendency relying on carbohydrate utilization is reduced and the utilization of dépot fat is begun smoothly in the early period of fasting.

Thus, it can be concluded that a prolonged supply of fat adapts the organism to fat utilization.

HIKASA et al. call this fact "fat adapting effect"[17)18)]. From this standpoint, it is well recognized that the fat given preoperatively improved the disturbances of fat metabolism after gastrectomy as follows: By means of the previous supply of fat the organism gains the fat adapting effect which makes the stress of operation much milder and minimizes metabolic disorders. It is quite reasonable that the preoperative administration of fat played a most important role in such a case, but not vitamins.

Though vitamins are indispensable in the effective oxidation of fat,[10)23)] they do not contribute to the gaining of the above-mentioned fat adapting effect.

When patients are forced to withstand a fasting or stressful state such as a postoperative period, they have to utilize effectively their own stored fat for a caloric source. Therefore, estimating such a stressful state, an ample preoperative supply of fat is a most reasonable procedure to make the organism adaptable to the utilization of fat more effectively. Consequently, it aids recovery of the living function after operation.

The question still remains unanswered as to how such adaptative alteration is induced in the metabolic pattern.

Concerning this problem SAMUELS et al. have merely postulated that some modification of the specific enzyme systems may possibly contribute to it.[37)]

Its relationship to the hormonal function should also be given consideration. In other words, it is highly possible that an alteration of the hormonal balance may contribute to the above adaptative metabolic pattern.

MATSUDA has already proven that changes in the liver glycogen content in starved rats has an intimate relationship with the adrenocortical function, and verified histochemically that the exhaustion of adrenocortical function was induced earlier in the fat free group. On the contrary, in animals which were well fortified by fat feeding it began gradually and the adrenocortical capacity of these was well preserved for a significantly longer period of starvation.[25]

On this occasion, it is necessary to consider not only such a favourable effect of the fat administration on the adrenocortical function, but also an action of the essential fatty acids which was contained in the fat emulsion abundantly.

It has been generally accepted that a main precursor of all kinds of steroid hormones is the cholesterol-ester existing in the adrenal cortex, and the essential fatty acids have an intimate relationship with the cholesterol metabolism.

JINDO,[21] TAMAKI[45] and MAKI[24] reported that the essential fatty acids were contained abundantly in the adrenal cortex. In these respects, it may reasonably be postulated that the essential fatty acids play an important role in the production of adrenal cortical hormones.

Moreover, NAGASE[27] proved that essential fatty acid deficiency causes an abnormal increase in capillary permeability predisposing to edema formation, and a weakend adrenocortical function may contribute to this phenomenon.

From the foregoing discussion and the results of the present experiment, it should be considered that a previous supply of fat, which prevents essential fatty acids deficiency inevitably, can be expected to display a favourable effect on the adrenocortical function and strengthens the resisting ability of the organism against stress. Moreover, by means of the stress moderating effect caused by the "fat adapting effect", the organism can be protected from the postoperative metabolic disorders of fat better than any other means.

Up to the present, it has generally been recognized that an abundant administration of fat should be prohibited in surgical cases, because it causes the lipemia and damages the liver function. However, the recent studies on the nutritional significance of fat confirm the fact that this liver damaging effect of fat is mostly due to the indiscriminate use of fat and the harm of fat can be completely excluded by using a properly selected fat, such as refined sesame oil which does not contain highly unsaturated fatty acids or auto-oxidation products, but is rich in the essential fatty acids.

In the present experiments, we may conclude that the improvement of the phospholipid formation from glycerides is induced partly by these favourable effect of fat upon liver function.

Furthermore, the advantages of the preoperative administration of fat have been proven by the protein sparing effect of fat[9] and the accelerating action of wound healing.[22]

Recently, it has become gradually recognized that the basic constituent element of tissue cells is lipoprotein. Therefore, enough fat of good quality has to be supplied in addition to protein in surgical cases in which the repair and reconstruction of tissue cells must be mainly expected.

Furthermore, in order to exclude the accumulation of fat intermediates, it is a very reasonable management that adequate amounts of carbohydrates, salts, vitamins and lipotropics are administered with fat and protein simultaneously.

V. CONCLUSION

In order to clarify the metabolic disorders following an operative insult such as a gastrectomy, the formation of phospholipids from the infused glycerides in vivo and the introduction of phospholipids labeled with P^{32} into tissues were investigated using a 20% sesame oil emulsion produced in our laboratory and radioactive phosphorus as a tracer, and the following results were obtained:

1) An operative insult caused by gastrectomy and subsequent starvation stress disturbs the metabolic process of fat in vivo, especially the formation of phospholipid from the infused glycerides to some degree.

2) Not all of these postoperative changes in fat metabolism can be regarded as a stress response. Some of them are the results of deficient preoperative nourishment.

3) These postoperative disturbances in fat metabolism are improved markedly by the repeated administration of the fat emulsion for one week before operation.

4) The preoperative administration of vitamins is not effective in producing this improvement.

5) Active supply of fat for some period prior to operation is an essential procedure for securing complete nutrition in surgical cases, because the organism relies upon its own dépot fat for a source of energy during operation and subsequent fasting.

Acknowledgement: The author wishes to express his sincere gratitude to Dr. Y. Hikasa, the lecturer of our clinic, for his valuable suggestions and kind guidance in the course of the work. He also wishes to express his thanks to Dr. T. Hiroshige, Director of Shinko Hospital, Dr. H. Hashino, and Dr. M. Inoue, Chief of Shinko Hospital, for their kind advice and encouragement.

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和 文 抄 録

手術前後に於ける脂質投与の妥当性についての実験的検討

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われわれの教室に於て創製された静脈内注入可能な脂質乳剤と，放射性P32を駆使応用することによつて，胃切除という外科的侵襲が生体に加えられた際，果たしてどの程度の脂質代謝障害が術後に惹起されるものであるかを，生体内に於けるグリセライドからのphospholipid生成能及びP32表示燐脂質の組織中への移行量から観察し，又その障害を軽減するには如何なる手段をとるべきかを実験的に明らかにし次のような結論を得た．

1) 胃切除という手術侵襲とそれに伴う飢餓ストレスは，生体内の脂質代謝過程，特にグリセライドからの phospholipid 生成能をある程度まで障害する．

2) 併しこのような現象は，単なるstress responseとして解釈すべきものではなくて，その招来される所以は術前の栄養管理の不備に帰すべきものである．

3) 即ち，このような術後に招来される脂質代謝障害は，予め術前1週間に亘つて脂質を前投与することによつて著明に改善される．

4) 而もその改善に当つては，術前に於いてのビタミン類投与は，何等の役割を演じていない．

5) 更に，生体に手術侵襲とそれにひきつづいて招来される飢餓ストレスが加えられる際，その時の主な熱源が貯蔵脂質の動員によつて賄れるものであるから，術前一定期間に亘つて予め脂質を積極的に投与することは，外科的侵襲を行うにさきだつて常に必ず行われなければならない必要な準備処置であると云つてよいであろう．